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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,572	07/10/2001	Avi Ashkenazi	GNE.1618P2C40	5445

30313 7590 02/26/2003

KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 02/26/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/902,572

Applicant(s)

ASHKENAZI ET AL.

Examiner

Gerald G Leffers Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 July 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a preliminary amendment, filed 7/10/01, in which claims 1-38 were cancelled and in which claims 39-44 were added. Claims 39-44 are pending in the instant application.

Information Disclosure Statement

It is noted that the file jacket indicates that an information disclosure statement was filed 04-11-02 as Paper No. 3. This document does not appear to be actually present in the file itself. Submission of a copy of the PTO Form 1449 filed on 04/11/02 and its corresponding references cited therein, would be remedial if applicants' wish the references to be considered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 39-44 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Each of the claims is directed towards an antibody that binds to the polypeptide described by SEQ ID NO: 255. The antibody can be a fragment that binds to SEQ ID NO: 255. The antibody can be a monoclonal antibody. The antibody can be labeled. The antibody can be humanized. The antibody can "specifically" bind to the polypeptide shown in SEQ ID NO: 255. Any utility for the claimed antibodies must be specific and substantial, or well established, for the protein encoded by SEQ ID NO: 255. Utilities simply directed to detection of, or purification

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of, the protein described by SEQ ID NO: 255 cannot be considered as substantial (i.e. having a “real-world” use) in the absence of a specific and substantial, or well-established utility for the protein to which the antibody binds. No such specific and substantial or well-established utility has been described for the protein described by SEQ ID NO: 255.

SEQ ID NO: 255 appears to have been novel in the art at the time of filing. Likewise, the nucleic acid sequence disclosed by applicants as encoding SEQ ID NO: 255, SEQ ID NO: 254, likewise appears to be novel in the art. Therefore, there is no well-established utility for the disclosed protein or antibodies specific for the protein.

The specification asserts that, based upon BLAST and FastA sequence analysis, various portions of PRO302 have significant homology with various protease proteins (page 110, top paragraph). Exactly which portions have homology to which portions of which other known proteases is not taught, however. Based upon the assertion that PRO302 comprises proteolytic activity, the specification asserts that PRO302 has utility in vivo for therapy as well as in vitro utilities. There is no indication in the specification that the supposed protease has any *specific* target for its supposed activity (e.g. association with a particular disease or specific substrate). There is no specific disease or condition shown in the prior art or instant specification to be associated with the protein described by SEQ ID NO: 255.

It is not likely that one of skill in the art could reasonably predict based upon the primary sequence of SEQ ID NO: 255 what specific activity PRO302 may have. The relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that

“Thus, one of the “grand challenges” of high-performance computer-predicting the structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain.” (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning protein structure, and failures to make it predictable. Thus, as taught by Berendsen, it is unlikely that one could predict the structural/functional characteristics of PRO302 based upon primary sequence alone. Further supporting Berendsen’s teachings, Galparin et al (Nature Biotechnology, Vol. 18, pages 609-613, June 2000; see the entire reference) teach that “sequence comparison methods, even the best ones, are of little help when a protein has no homologs in current databases or when all database hits are to uncharacterized gene products.” Galperin et al disclose that “assessing the actual power of the context based method for protein function prediction requires extensive testing by labor-consuming, case-by-case, computational, and eventually experimental analysis.” Attwood (Science, Vol. 290, pages 471-473, see the entire reference) also states that it is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences.” It is clear from the cited references that one cannot reliably predict based upon primary structure alone or on mere sequence homology what specific activity PRO302 might possess.

The specification does teach in Example 85 that the PRO302 protein has an effect on vascular leakage when injected into hairless guinea pigs. While the specification concludes that PRO302 protein can induce vascular permeability in the guinea pig model, it does not give the actual data or an indication of the relative activity of the PRO302 protein compared to the positive control. In addition to not providing a basis for one of skill in the art to determine the

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actual effectiveness of PRO302 in inducing vascular permeability, the specification does not provide a basis to envision a specific, real-world application for the asserted ability to induce vascular permeability. It is further noted that the observed activity is not unique to PRO302 in that at least one other protein and the positive control both induced vascular permeability in the guinea pig model. Based on these teachings, one of skill in the art at the time of applicants' invention would not be able to recognize a specific utility (e.g. specific proteolytic substrate) or substantial utility (i.e. not requiring additional research in order to confirm a real-world application for the claimed proteins) for the claimed proteins. Because no specific and substantial or well-established utility has been demonstrated for the protein described by SEQ ID NO: 255, one of skill in the art would not have been able to recognize a specific and established utility for the claimed antibodies.

Claims 39-44 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 44 is vague and indefinite in that the metes and bounds of the words "specifically binds to" are unclear. The phrase does not appear to be explicitly defined in the specification and makes it unclear the nature and degree of the characteristics required for an antibody to bind "specifically" to a given protein. Does the phrase mean that the antibody only binds to the recited PRO32 protein and no other proteins? Does it refer to the strength of binding? Does the phrase mean that the antibody only binds a few other proteins? It would be remedial to amend the claim language to explicitly set forth the nature and degree of the characteristics required for the claimed antibody to bind "specifically" a given protein.

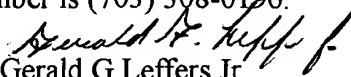
Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
February 24, 2003